§1.821-1.825. Enclosed herewith in full compliance with 37 C.F.R. 1.821-1.825 is a Sequence Listing to be inserted into the specification as indicated above. The Sequence Listing in no way introduces new matter into the specification.

Also submitted herewith in full compliance with 37 C.F.R. 1.821-1.825 is a disk copy of the Sequence Listing. The disk copy of the Sequence Listing, file "1209-121.app", is identical to the paper copy, except that it lacks formatting. Withdrawal of the objection is, therefore, respectfully requested.

**Rejections under 35 U.S.C. §112, second paragraph**

The claims have been rejected under 35 U.S.C. §112, second paragraph as being indefinite, for the following reasons.

1) Claims 1-8, have been rejected for recitation of "characterized in that."

2) Claims 6 and 7 have been rejected as being unclear in the respective recitation of "crosslinkable oligonucleotides" and "a ligase is added" with the assertion that it is not clear whether the addition of the ligase is a positive effect.

3) Claim 8 has been rejected for recitation of "an oligonucleotide complementary to the crosslinkable .oligonucleotides of claims 6 or 7...,"

4) Claim 6 has been further rejected for recitation of "amplifying said crosslinked oligonucleotides" with the assertion that it is no clear when or how the oligonucleotides became crossslinked.

5) Claims 1 and 4 have been rejected for being drawn to an immunological test kit, but failing to recite an antibody.

6) Claim 3 has been rejected as being unclear and improperly reciting a Markush group.

The claims have been amended as indicated above to address the rejections raised by the Examiner and clarify the scope of the claims. As the above amendments address the rejections of the claims as being indefinite, withdrawal of the rejections is respectfully requested.

**Rejections under 35 U.S.C. §102**

Claims 1-5 have been rejected as being anticipated by or being obvious over Urdea et al. (U.S. Patent No. 5,656,731). Urdea et al. is asserted to teach nucleic acid-amplified immunoassay reagents in the kits of the present invention. Ureda et al. is further asserted to differ from the present invention only in failing to claim the reagents as a kit.

Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The present invention is drawn to a test kit comprising

a) a first immobilized reagent having affinity to a specific macromolecule, and

b) a second and a third affinity reagent specific for different determinants of said macromolecule, and modified with crosslinkable oligonucleotides.

Ureda et al. disclose reagents wherein an analyte specific domain has been combined with a nucleic acid sequence. This combination allows signal amplification through the transcription of the nucleic acid sequence. The present invention relies on the concept of a signal being generated when two detection probes are bound sufficiently close to each other. There is no disclosure or suggestion in Ureda et al. of creating a signal by the ligation of two sufficiently closely bound detection probes. The ligation reaction disclosed in Ureda et al. pertains to the manufacture of the probe, not to the assay conditions/reactions. As such the present invention is distinct from and not obvious over Ureda et al. Withdrawal of the rejection is therefore, respectfully requested.

Claims 1, and 3-5 have been rejected as being anticipated by or obvious over Birkenmeyer et al. (U.S. Patent No. 5,667,974). Birkenmeyer et al. is asserted to teach the use of the affinity reagents in kits of the present invention. The Examiner asserts Birkenmeyer et al. differ from the present invention in failing to claim kits containing the reagents. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Birkenmeyer et al. is drawn to a method of detecting nucleic acids. There is no disclosure in Birkenmeyer et al. of a general kit for detecting molecules other than nucleic acid. Nor is there a disclosure of the principle by which the presently claimed kit functions, i.e. that simultaneous recognition of two or more determinants are required to amplify the signal. As such, the present invention is clearly not anticipated by or obvious over Birkenmeyer et al. Withdrawal of the rejection is therefore, respectfully requested.

**Rejections under 35 U.S.C. §103**

Claims 1 and 3-5 have been rejected under 35 U.S.C. §103 as being obvious over Nickerson et al, Delahunty et al., Kwok et al. or Nilsson et al. The cited references are asserted to

teach the reagents of the present invention. The Examiner asserts it would be obvious to include the reagents in the presently claimed kits. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

Firstly, Nickerson et al. regards the sequencing of DNA to identify genetic polymorphisms. Clearly, DNA sequencing has no relationship to the present invention. The disclosure of Nickerson et al. references to oligonucleotide ligation assay (OLA) of Delahunty et al. and Kwok et al. Both the OLA assay and the "padlock" probes of Nilsson et al. regard methods of analyzing DNA sequences. In the references, ligation is used to distinguish differences in the DNA sequences that the probes have hybridized to. In the present invention, it is the binding of the affinity probes which juxtaposes the oligonucleotides, which can then be amplified. With the present invention, oligonucleotide ligation is a means of detecting closely located probe-binding sites. This concept is completely different than that of Nickerson et al, Delahunty et al., Kwok et al. or Nilsson et al., where DNA sequences are analyzed through sequence ligation. There is no sequence analysis with the present invention. There is no suggestion in Nickerson et al, Delahunty et al., Kwok et al. or Nilsson et al. of detecting

macromolecules, such as protein antigens, through the ligation of oligonucleotides. As such, the present invention is clearly not obvious over Nickerson et al, Delahunty et al., Kwok et al. or Nilsson et al.

Claims 1-2 and 6 have been rejected under 35 U.S.C. §103 as being obvious over Lee et al. in view of Dattagupta et al. (U.S. Patent No. 4,748,111). Lee et al. is asserted to disclose an immunometric assay suing an immobilized antibody and two or more soluble antibodies. Lee et al. is asserted to differ from the present invention in failing

As the above-presented amendments and remarks address and overcome the rejections of the Examiner, withdrawal of the rejections and reconsideration and allowance of the claims are respectfully requested. Should the Examiner have any questions regarding the present application, he is requested to contact MaryAnne Liotta, PhD (Reg. No. 40,069) in the Washington DC area, at (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any

additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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